

Figure 1

CD95

>sp|P25445|TNR6_HUMAN Tumor necrosis factor receptor superfamily member 6 precursor (FASL receptor) (Apoptosis-mediated surface antigen FAS) (Apo-1 antigen) (CD95) - Homo sapiens (Human).

1 MLGIWTLLPL VLTSVARLSS KSVNAQVTDI NSKGLELRKT VTTVETQNLE GLHHGDQFCH
61 KPCPPGERKA RDCTVNGDEP DCVPCQEGKE YTDAHFSSK CRRCRLCDEG HGLEVEINCT
120 RTQNTKCRCK PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS RSNLGWLCLL
180 121
181 LLPIPLIVWV KRKEVQKTCR KHRKENQGSH ESPTLNPETV AINLSDVDLS KYITTIAGVM
240 241
300 TLSQVKGFVRLNGVNEAKID EIKNDNVQDT AEQKVQLLRN WHQLHKGKEA YDTLIKDLKK
301 335
ANLCTLAEKI OTIILKDIS DSENSNFRNE IQSLV

AA 1-16 Signal peptide (potential)
AA 17-173 extracellular domain (potential)
AA 47-83 CRD1
AA 84-127 CRD2.
AA 128-166 CRD3
AA 174-190 transmembrane (potential)
AA 191-335 cytoplasmic (potential)

Figure 2

IgG1

>sp|P01857|GC1_HUMAN Ig gamma-1 chain C region - Homo sapiens (Human).

1 60
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFFPAVLQSS
61 120
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG
121 180
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN
181 240
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE
241 300
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTPPV LDSDGSFFLY SKLTVDKSRW
301 330
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK

AA 99-110 hinge region

AA 111-223 CH2 region

AA 224-330 CH3 region

Variants D239E, L241M

Figure 3A**CD95-Fc (AA 1-172 CD95 and AA 102-330 IgG1)**

1 MLGIWTLPL VLTSVARLSS KSVNAQVTDI NSKGLELRKT VTTVETQNLE GLHHGDQFCH 60
 61 KPCPPGERKA RDCTVNGDEP DCVPCQEGKE YTDKAHFSSK CRRCRLCDEG HGLEVEINCT 120
 121 RTQNTKCRCK PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS RSCDKTHTCP 180
 181 PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA 240
 241 KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTI S KAKGQPREPQ 300
 301 VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTPPV LDSDGSFFLY 360
 361 SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 400

Figure 3B

Example of a preferred CD59-Fc fusion protein with an overlapping amino acid:

CD95 extracellular domain	huIgG1
131 PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS R <u>S</u> N	173 99 120 EP K <u>S</u> CDKTHTCP PCPAPELLGG
PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS R <u>S</u> CDKTHTCP PCPAPELLGG	

Figure 4**3. TRAIL-R1**

>sp|000220|T10A_HUMAN Tumor necrosis factor receptor superfamily member 10A precursor (Death receptor 4) (TNF-related apoptosis-inducing ligand receptor 1) (TRAIL receptor-1) (TRAIL-R1) - Homo sapiens (Human).

1 MAPPPARVHL GAFLAVTPNP GSAASGTEAA AATPSKVVGS SAGRIEPRGG GRGALPTSMG 60
61 QHGPSARARA GRAPGPRPAR EASPRLRVHK TFKFVVVGVL LQVVPSSAAT IKLHDQSIGT 120
121 QOWEHSPPLGE LCPPGSHRSE HPGACNRCTE GVGYTNASNN LFACLPCTAC KSDEEERSPC 180
181 TTTTRNTACQC KPGTFRNDNS AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHNI 240
241 300
241 WVILVVTLVV PLLLVAVLIV CCCIGSGCGG DPKCMDRVCF WRLGLLRGPG AEDNAHNEIL 360
301 360
361 SNADSLSTFV SEQQMESQEP ADLTGVTVQS PGEAQCLLGP AEAEGSQRRR LLVPANGADP 420
421 420
TETLMLFFDK FANIVPFDSW DQLMRQLDLT KNEIDVVRAG TAGPGDALYA MLMKWVNKTG 468
468
RNASIHTLLD ALERMEERHA KEKIQDLLVD SGKFIYLEDG TGSAVSLE

AA 1-23 Signal peptide (potential)
AA 24-239 extracellular domain (potential)
AA 107-145 CRD1
AA 147-188 CRD2
AA 189-229 CRD3
AA 240-262 transmembrane (potential)
AA 263-468 cytoplasmic (potential)

Figure 5

Examples of Trail-R1-Fc fusion proteins with overlapping amino acids:

Trail R1 extracellular domain		huIgG1
201 AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S GN G H _N	239	99 120 EP KSCDKTHTCP PCPAPELLGG
		AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S EP KSCDKTHTCP PCPAPELLGG
201 AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S GN G H _N	239	99 120 EP KSCDKTHTCP PCPAPELLGG
		AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S CDKTHTCP PCPAPELLGG
201 AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S GN G H _N	239	99 120 EP KSCDKTHTCP PCPAPELLGG
		AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKE S GN G H _N TCP PCPAPELLGG

Figure 6**4. TRAIL-R2 (long)**

>sp|014763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

1 MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVS AESALITQQD 60
61 LAPQQQRAAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD 120
121 SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRKCRTGC PRGMVKVGDC TPWSDIECVH 180
181 KESGTKHSGE APAVEETVTS SPGTPASPCS LSGIIIGVTV AAVVLIVAVF VCKSLLWKKV 240
241 LPYLIKICSG GGGDPERVDR SSQRPGGAEDN VLNEIVSILQ PTQVPEQEME VQEPAEPTGV 300
301 NMLSPGESEH LLEPAEAERS QRRRLLVPAN EGDPTETLRQ CFDDFADLVP FDSWEPLMRK 360
361 LGLMDNEIKV AKAEEAAGHRD TLYTMLIKWV NKTGRDASVH TLDALETLG ERLAKQKIED 420
421 440
HLLSSGKFMY LEGNADSAMS

AA 1-55 Signal peptide
AA 56-210 extracellular domain (potential)
AA 57-94 CRD1
AA 97-137 CRD2
AA 138-178 CRD3
AA 192-206 TAPE
AA 211-231 transmembrane (potential)
AA 232-440 cytoplasmic (potential)

Figure 7

Examples of Trail-R2 (long)-Fc fusion proteins with overlapping amino acids ("repeat" included):

Trail R2 (long) extracellular domain		huIgG1
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		
Bevorzugte Ausführung (wie in EP 03006949.6 beschrieben)		
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		
171 TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S	210	99 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPC _S CDKTHTCP PCPAPELLGG		

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Figure 8

Examples of Trail-R2(long)-Fc fusion proteins with overlapping amino acids ("repeat" not included):

Trail R2 (long) extracellular domain	huIgG1	
171 191 TPWSDIECVH KESG T KHSGE A	99	120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESG T KHSGE P KSCDKTHTCP PCPAPELLGG		
171 191 TPWSDIECVH KESG T KHSGE A	99	120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESG T KH S CDKTHTCP PCPAPELLGG		
171 191 TPWSDIECVH KESG T KHSGE A	99	120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESG T KH S CDKTHTCP PCPAPELLGG		
171 191 TPWSDIECVH KESG T KHSGE A	99	120 EP KSCDKTHTCP PCPAPELLGG
TPWSDIECVH KESG T KH S CDKTHTCP PCPAPELLGG		

Figure 9**5. TRAIL-R2 (short)**

>sp|014763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

1 MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVS AESALITQQD 60
61 LAPQQRAAPQ QKRSSPSEG CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD 120
121 SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRKCRTGC PRGMVKVGDC TPWSDIECVH 180
181 KESGIIIGVT VAAVVLIVAV FVCKSLLWKK VLPYLGICS GGGGDPERVD RSSQRPGaed 240
241 NVLNEIVSIL QPTQVPEQEM EVQEPAEPTG VNMLSPGESE HLLEPAAER SQRRRLLVPA 300
301 NEGDPTETLR QCFDDFADLV PFDSWEPLMR KLGLMDNEIK VAKAEAAGHR DTLYTMLIKW 360
361 VNKTGRDASV HTLLDALETL GERLAKQKIE DHLLSSGKFM YLEGNADSAM S 411

AA 1-55 Signal peptide
AA 56-184 extracellular domain (potential)
AA 57-94 CRD1
AA 97-137 CRD2
AA 138-178 CRD3
AA 213-202 transmembrane (potential)
AA 203-411 cytoplasmic (potential)

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Figure 10

Examples of Trail-R2(short)-Fc fusion proteins with overlapping amino acids:

Trail-R2 (short) extracellular domain		huIgG1
151	184	99
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KEP KSCDKTHTCP PCPAPELLGG		
151	184	99
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		120 EP K SCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH K SCDKTHTCP PCPAPELLGG		
151	184	99
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		120 EP K SCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KES CDKTHTCP PCPAPELLGG		
151	184	99
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KESG		120 EP K SCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKVGDC TPWSDIECVH KES CDKTHTCP PCPAPELLGG		

Figure 11

6. TRAIL-R3

>sp|014798|T10C_HUMAN Tumor necrosis factor receptor superfamily member 10C precursor (Decoy receptor 1) (DcR1) (Decoy TRAIL receptor without death domain) (TNF- related apoptosis-inducing ligand receptor 3) (TRAIL receptor-3) (TRAIL-R3) (Trail receptor w

1 MARIPKTLKF VVVIVAVLLP VLAYSATTAR QEEVPQQTVA PQQQRHSFKG EECPAGSHRS 60
61 120
EHTGACNPCT EGVDYTNASN NEPSCFPCTV CKSDQKHKS CTMTRDTVCQ CKEGTFRREN
121 180
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE TPAAEETMNT SPGTPAPAAE
181 240
ETMNTSPGTP APAAEETMTT SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPASSHY
241 259
LSCTIVGIIV LIVLLIVFV

AA 1-23 Signal peptide
AA 24-236 extracellular domain
AA 29-66 CRD1
AA 69-109 CRD2
AA 110-149 CRD3
AA 162-236 5 x 15 AA tandem tape repeats
AA 237-259 removed in mature form (potential)

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Figure 12

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids ("repeats" included):

Trail-R3 extracellular domain		hIgG1
201 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	236	99 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA		KSCDKTHTCP PCPAPELLGG
201 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	236	99 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA		KSCDKTHTCP PCPAPELLGG
201 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	236	99 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA		KSCDKTHTCP PCPAPELLGG
201 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	236	99 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA		KSCDKTHTCP PCPAPELLGG
201 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	236	99 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA		KSCDKTHTCP PCPAPELLGG

Figure 13

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids ("repeats" not included):

Trail-R3 extracellular domain		huIgG1
121	161	99 120
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V E T		EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V EP KSCDKTHTCP PCPAPELLGG		
121	161	99 120
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V E T		EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EE P KSCDKTHTCP PCPAPELLGG		
121	161	99 120
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V E T		EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V EP KSCDKTHTCP PCPAPELLGG		
121	161	99 120
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V E T		EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V HTCP PCPAPELLGG		
121	161	99 120
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V E T		EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQC V EEFGANAT V HTCP PCPAPELLGG		

Figure 14**7. TRAIL-R4**

>sp|Q9UBN6|T10D_HUMAN Tumor necrosis factor receptor superfamily member 10D precursor (Decoy receptor 2) (DcR2) (TNF-related apoptosis-inducing ligand receptor 4) (TRAIL receptor-4) (TRAIL-R4) (TRAIL receptor with a truncated death domain) - Homo sapiens

1 MGLWGQSVPT ASSARAGRYP GARTASGTRP WLDPKILKF VVFIVAVLLP VRVDSATIPR 60
61 QDEVPPQQTVA PQQQRRSLKE EECPAGSHRS EYTGACNPCT EGVDYTIASN NLPSCLLCTV 120
121 CKSGQTNKSS CTTTRDTVCQ CEKGSFQDKN SPEMCRTCRT GCPRGMVKVS NCTPRSDIKC 180
181 240
KNESAASSTG KTPAAEETVT TILGMLASPY HYLIIIVLV IILAVVVVGF SCRKKFISYL 300
241 360
KGICSGGGGG PERVHRVLFR RRSCPDRVPG AEDNARNETL SNRYLQPTQV SEQEIQGQEL
301
AELTGVTVES PEEPQRLLEQ AEAEGCQRRR LLVPVNDADS ADISTLLDAS ATLEEGHAKE
361 386
TIQDQLVGSE KLFYEEDEAG SATSCL

AA 1-55 signal peptide
AA 56-211 extracellular domain (potential)
AA 58-97 CRD1
AA 98-139 CRD2
AA 140-180 CRD3
AA 212-232 transmembrane (potential)
AA 233-386 cytoplasmic (potential)

Figure 15

Examples of Trail-R4-Fc fusion proteins with overlapping amino acids:

Trail-R4 extracellular domain		huIgG1
171 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	211	99 120 EP KSCDKTHTCP PCPAPELLGG
		NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY KSCDKTHTCP PCPAPELLGG
171 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	211	99 120 EP KSCDKTHTCP PCPAPELLGG
		NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASCDKTHTCP PCPAPELLGG
171 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	211	99 120 EP KSCDKTHTCP PCPAPELLGG
		NCTPRSDIKC KNESAASSTG KTPAAEETVT THTCP PCPAPELLGG
171 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	211	99 120 EP KSCDKTHTCP PCPAPELLGG
		NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY HTCP PCPAPELLGG

Figure 16

1. TNF-R1

>sp|P19438|TR1A_HUMAN Tumor necrosis factor receptor superfamily member 1A precursor (p60) (TNF-R1) (p55) (CD120a) [Contains: Tumor necrosis factor binding protein 1 (TBPI)] - Homo sapiens (Human).

1 60
MGLSTVPDLL LPLVLLELLV GIYPSGVIGL VPHLGDRREKR DSVCPQGKYI HPQNNSICCT
61 120
KCHKGTYLYN DCPGPGQD TD CRECESGSFT ASENHLRHCL SCSKCRKEMG QVEISSCTVD
121 180
RDTVCGRKN QYRHYWSEN L FQCFNCSLCL NGTVHLSCQE KQNTVCTCHA GFFLRENECV
181 240
SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT TVLLPLV IFF GLCLLSLLFI GLMYRYQRWK
241 300
SKLYSIVCGK STPEKEGELE GTTTKPLAPN PSFSPTPGFT PTLGFSPVPS STFTSSSTYT
301 360
PGDCPNFAAP RREVAPPYQG ADPILATALA SDPIPPLQK WEDSAHKPQS LDTDDPATLY
361 420
421 455
AVVENVPPLR WKEFVRRRLGL SDHEIDRLEL QNGRCLREAQ YSMLATWRRR TPRREATLEL
LGRVLRDMDL LG CLEDIEEA LCGPAALPPA PSLLR

AA 1-21 Signal peptide
AA 22-211 extracellular domain (potential)
AA 43-82 CRD1
AA 83-125 CRD2
AA 126-166 CRD3
AA 167-196 CRD4
AA 212-234 transmembrane (potential)
AA 235-455 cytoplasmic (potential)

Figure 17

Examples of TNF-R1-Fc fusion proteins with overlapping amino acids:

TNF-R1 extracellular domain		huIgG1
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		
171	211	99 120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT T EP KSCDKTHTCP PCPAPELLGG		
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTEP KSCDKTHTCP PCPAPELLGG		

Figure 18

2. TNF-R2

>sp|P20333|TR1B_HUMAN Tumor necrosis factor receptor superfamily member 1B precursor (Tumor necrosis factor receptor 2) (p80) (TNF-R2) (p75) (CD120b) (Etanercept) [Contains: Tumor necrosis factor binding protein 2 (TBPII)] - Homo sapiens (Human).

1 MAPVAVWAAL AVGLELWAAA HALPAQVAFT PYAPEPGSTC RLREYYDQTA QMCCSKCSPG 60
61 QHAKVFCTKT SDTVCDSCED STYTQLWNWV PECLSCGSRC SSDQVETQAC TREQNRICTC 120
121 RPGWYCALSK QEGCRLCABL RKCRPGFGVA RPGTETSDVV CKPCAPGTFS NTTSSSTDICR 180
181 PHQICNVVAI PGNASMDAVC TSTS PTRSMA PGAVHLPQPV STRSOHTOPT PEPSTAPSTS 240
241 FLLPMGPSPP AEGSTGDFAL PVGLIVGVTA LGLLIIGVVN CVIMTQVKKK PLCLQREAKV 300
301 PHLPADKARG TQGPEQQHLL ITAPSSSSSS LESSASALDR RAPTRNQPQA PGVEASGAGE 360
361 ARASTGSSDS SPGGHGTQVN VTCIVNVCSS SDHSSQCSSQ ASSTMGDTDS SPSESPKDEQ 420
421 VPFSEECAF RSQLETPETL LGSTEKPLP LGVPDAGMKP S 461

AA 1-22 Signal peptide
AA 23-257 extracellular domain (potential)
AA 39-76 CRD1
AA 77-118 CRD2
AA 119-162 CRD3
AA 163-201 CRD4
AA 258-287 transmembrane (potential)
AA 288-461 cytoplasmic (potential)

Figure 19

Examples of TNF-R2-Fc fusion proteins with overlapping amino acids:

TNF-R2 extracellular domain		huIgG1
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEP KSCDKTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD KTHTCP PCPAPELLGG		
221	257	99 120
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		
		EP KSCDKTHTCP PCPAPELLGG
STRSQHTQOPT PEPSTAPSTS FLLPMGPSPP AEGSTGD KTHTCP PCPAPELLGG		